Clinical Pathologist's Easy Chair

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WBC Differential

The WBC differential is the relative frequency of the white blood cell types in peripheral blood. It is usually ordered to identify any abnormality that may be present in the blood smear or to compare the current WBC population with a previous study. When a WBC differential is done, we assume that the leukocyte distribution in the blood smear corresponds to that in the patient; a random sample of the cells in the smear is examined, and the cells are correctly identified.

The WBC differential is one of the most frequently requested and often overused laboratory procedures. The request for a differential is often "automatic" and ordered when only a hemoglobin or total WBC is desired. The differential is a labor-intensive procedure and the available automated systems do *not* identify all cells nor distinguish such details as the difference between bands and segmented neutrophils. The usual textbook normal adult leukocyte count, first obtained from a study of 105 medical students, is given as 5,000 to 10,000 per μL with 95% statistical limits of 4,860 to 10,700 and the normal differential is as follows[1]:

Segmented neutrophils:
25% to 69% or 1450 to 5890/μL
Juvenile and Band neutrophils:
0% to 17% or ≤1450/μL
Lymphocytes:
21% to 49% or 1490 to 3920/μL
Monocytes:
2.5% to 10.5% or 140 to 860/μL
Eosinophils: 0% to 7% or ≤ 570/μL
Basophils: 0% to 1.6% or ≤ 124/μL

The differential is usually reported in percent but the total number per μL may be more meaningful when the total leukocyte level is above or below the normal range. Studies of larger groups of healthy adults have shown a normal total leukocyte count of 4,100 to 10,900 per μL[2] and bands up to 2,100 per μL with an average of 600[3].

The classification of bands is a continuing problem because many observers still include some of the bands in the segmented neutrophil category. The difference between a band and segmented neutrophil is seen at the connection between the lobes of the nucleus. The lobes of the band nucleus have nuclear material between 2 distinct membranes whereas the segmented neutrophil has nuclear lobes connected by a thread-like filament that is so narrow there is no visible chromatin[4]. Bands are not separately identified and are counted as segmented neutrophils in the automated differential. Myelocytes are not normally found in the peripheral blood smears but may be seen in buffy coat smears.

There are a number of factors other than disease that can alter the WBC differential. These include a combination of analytical and sampling variability and physiological changes. More than 750 of the total variance in the neutrophils, lymphocytes, monocytes and basophils and about 50% of the eosinophil variance are due to factors other than disease[5]. The patient's own daily variation is the best reference in assessing day-to-day changes.

Because of the chance distribution of cells in a smear, analytic variations for neutrophils is at least 10%, lymphocytes 15%, monocytes 48%, eosinphils 52% and basophils 141%. Much of the variation in the WBC differential is due to the obligatory random variation that depends upon the number of cells counted. The larger the number of cells examined, the narrower the confidence limits. The sampling variability, therefore, must be considered before deciding on the significance of any change in the differential[6].

Physiologic fluctuations of the leukocytes occur from day to day and during a single day. The total WBC count is usually higher in the afternoon and after heavy muscle activity, such as exercise and manual labor; but the diurnal variation for neutrophils, monocytes and lymphocytes is random and not systematic. Extremes of heat or cold, emotional states (excitement or depression), pregnancy, and some medications (steroids, digitalis, etc) are causes of leukocytosis. The diurnal variation in healthy subjects is 9.4% for total WBC, 12.9% for neutrophils, 10.3% for lymphocytes, 18.6% for monocytes, 20% for eosinophils and 7.4% for basophils[5].

Frequently repeated differentials are expensive and almost worthless. They should be limited to situations where the clinical course is not clear and at long enough intervals that the results can affect clinical decisions[7]. The differential is of no value if the patient is improving clinically and it probably will not change the management of the patient who is clinically deteriorating unless there are alternate modes of treatment.

Repeat differentials are usually ordered to:

1. Confirm a previously abnormal differential.
2. Evaluate and/or monitor selected chronic diseases:
   a. Myeloproliferative/ myelodysplastic disorders.
   b. Chronic infections.
   c. Systemic malignancies.
   d. Autoimmune diseases such as SLE.
3. Monitor therapy:
   a. Cancer chemotherapy.
   b. Drugs that suppress the bone marrow such as clindamycin, chloramphenicol, semi-synthetic penicillins, gentamicin and phenylbutazone.

The day-to-day change is considered significant when the highest value of a sequence of counts exceeds the lowest by 2 CV or 31% for the total WBC, and 46% for PMN (neutrophils)[8]. Another study concluded that the minimum significant change in the total count is 50% and for PMN was 46%[9]. Repeat differentials without a significant change in the total WBC would result in little or no information[10]. The total WBC adequately predicts changes in the neutrophils in 99% of instances. When there is a risk for leukopenia because of chemotherapy, the differential is not necessary if the total WBC is greater than 4,500 per μL—the total WBC correlates with the neutrophil count. If the total WBC is less than 500 to 1,000 per μL, the neutrophil count is too low to protect against

hospital-acquired infections and a repeat differential would not be helpful[7]. Repeat differentials at University of California Medical Center are *not* done unless there is a significant change in the total WBC; the authors suggest that a total WBC be done on alternate days or twice a week, and a differential only if the total WBC is *twice* or *one half* the original count[10]. They also suggest that all significant changes in the total count and differential be verified on the following day.

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Table of significant change of WBC differential[6].

Percentage of cells in initial count	Change not significant when second count in this range
1%	0 to 8%
5	0 to 14
10	2 to 21
15	6 to 27
20	9 to 33
25	12 to 39
30	17 to 44
35	22 to 49
40	26 to 55
45	31 to 60
50	36 to 64
55	40 to 69
60	45 to 74
65	51 to 78
70	56 to 83
75	61 to 87
80	67 to 90
85	73 to 94
90	79 to 98
95	86 to 100
100	92 to 100